

Applicants: Vadiraja Murthy and Edward R. Burns  
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originally filed. Accordingly, entry of Claim 19 is respectfully requested. Applicants maintain that the claims presently under examination, namely Claims 1-4, 8-10 and 19 define patentable subject matter and earnestly solicit allowance of these claims.

#### Reference to Parent Application

The Examiner required amendment of the specification to include a reference to the prior application and to the status of the parent application.

In response, applicants have hereinabove amended the specification to include a statement referring to the parent application and the status thereof.

#### 35 U.S.C. §112, First Paragraph Objection

The Examiner objected to the specification under 35 U.S.C. §112, first paragraph, as failing to provide an adequate written description of the invention.

In response, applicants have amended Figure 2 in the attached Amendment Pursuant to 37 C.F.R. §1.123 to include a label for the peak which represents adenylate kinase activity. Further, applicants have hereinabove amended the brief description of Figure 2 to refer to the label. No new matter is presented by the amendment to the specification. Accordingly, entry of this amendment is respectfully requested.

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35 U.S.C. §112, Second Paragraph Rejection

The Examiner rejected Claims 13-15 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In response, applicants have hereinabove canceled Claims 13-15 and added new Claim 19. New Claim 19 incorporates Claims 13-15 to more clearly set forth and define the invention. No new matter is presented by Claim 19. Accordingly, entry of Claim 19 is respectfully requested.

35 U.S.C. §103(a) Rejections of Claims 1-4

The Examiner rejected Claim 1 under 35 U.S.C. §103(a) as being unpatentable over Olsson, et al.; Claims 2 and 3 under 35 U.S.C. §103(a) as being unpatentable over Olsson, et al. as applied to Claims 1 and 13 in further view of Tsuji, et al., or Friedrich, et al., and, if necessary, further in view of Buth, et al.; and Claim 4 under 35 U.S.C. §103(a) as being unpatentable over Olsson, et al. as applied to Claims 1 and 13 in further view of Matsuura, et al..

Olsson, et al. describe an assay for measuring total adenylate kinase activity in plasma by measuring the formation of ATP from ADP using the firefly luciferase reaction. The assay described by Olsson, et al. detects all adenylate kinase activity,

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regardless of the origin of the adenylate kinase. The Olsson, et al. assay does not detect and distinguish erythrocytic adenylate kinase in serum, but detects only total adenylate kinase in plasma. The method described by the subject application, however, specifically detects erythrocytic adenylate kinase and distinguishes erythrocytic adenylate kinase from adenylate kinases of other origins in a serum sample.

The use of DAPP by Olsson, et al. as an inhibitor of erythrocytic adenylate kinase in a plasma sample also inhibits erythrocytic adenylate kinase released by platelets. The use of DAPP by Olsson, et al. does not teach or suggest detection of erythrocytic adenylate kinase in a serum sample with specificity and particularity as taught by the present invention.

Tsuji, et al., Friedrich, et al., and Buth, et al. describe methods for visualizing total adenylate kinase. The methods described by these references do not teach or suggest a method for detecting and distinguishing erythrocytic adenylate kinases from total adenylate kinase present in a serum sample as taught by the method of the present invention.

The addition of Matsuura, et al. does not remedy the deficiencies of Olsson, et al.. Matsuura, et al. describe a method for determining the amount of total adenylate kinase in a sample by immunoblot analysis. The anti-adenylate kinase antibody employed in this assay detects all adenylate kinases, regardless of the

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origin. The method described by Matsura, et al. does not teach or suggest a method for detecting erythrocytic adenylate kinase using an antibody that specifically binds to erythrocyte adenylate kinase in a serum sample as taught by the present invention.

35 U.S.C. §103(a) Rejections of Claims 8-10 and 13-15

The Examiner rejected Claims 13 and 14 under 35 U.S.C. §103(a) as being unpatentable over Olsson, et al.; Claim 15 under 35 U.S.C. §103(a) as being unpatentable over Olsson, et al. as applied to Claims 1 and 13 in further view of Tsuji, et al., or Friedrich, et al., and, if necessary, further in view of Buth, et al.; and Claims 8-10 under 35 U.S.C. §103(a) as being unpatentable over Olsson, et al. as applied to Claims 1 and 13 in further view of Matsuura, et al..

Claims 13-15 are combined into Claim 19 by this Amendment. Applicants assert that the cited references, taken alone or in combination, do not render the claims obvious.

Olsson, et al. describe an assay for measuring total adenylate kinase activity in plasma by measuring the formation of ATP from ADP using the firefly luciferase reaction. The assay described by Olsson, et al. measures only total adenylate kinase activity, regardless of the origin of the adenylate kinase. The Olsson, et al. assay does not specifically measure erythrocytic adenylate kinase activity. The method described by the subject

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application, however, measures with specificity and particularity the activity of erythrocytic adenylate kinase in a given serum sample.

The use of DAPP by Olsson, et al. as an inhibitor of erythrocytic adenylate kinase merely suggests that erythrocytic adenylate kinase of all origins, including platelets, is present in the plasma sample. Olsson, et al.'s use of DAPP does not determine the amount or activity of erythrocytic adenylate kinase in the sample.

The methods described by Friedrich, et al., Tsuji, et al., and Buth, et al. are all methods for visualizing total adenylate kinase and are not methods for determining the amount or activity of the adenylate kinase present in a sample. These methods simply confirm the presence of total adenylate kinase in a given sample, and do not quantify the amount of total adenylate kinase present, nor suggest the origin of the adenylate kinase. Accordingly, the methods described by Friedrich, et al., Tsuji, et al., and Buth, et al. do not teach or suggest a method of determining erythrocytic adenylate kinase with specificity and particularity as taught by the method of the present invention.

The addition of Matsuura, et al. does not remedy the deficiencies of Olsson, et al.. Matsuura, et al. describe a method for determining the amount of total adenylate kinase in a sample by immunoblot analysis. The anti-adenylate kinase antibody employed

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in this assay detects all adenylate kinase, regardless of the origin. The method described by Matsura, et al. does not teach or suggest a method for determining the specific amount and activity of erythrocytic adenylate kinase in a sample as taught by the present invention.

In view of the preceding amendments and remarks, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of rejection set forth in the May 19, 1997 Office Action, and earnestly solicit allowance of the pending claims.

If a telephone interview would further the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. If any fee, however, is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 01-1785.

Respectfully Submitted,

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Dated: June 25, 1997  
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Figure 2

